

**REMARKS**

Applicants have carefully considered this Application in connection with the Examiner's Office Action, and respectfully request reconsideration of this Application in view of the above amendments and the following remarks.

Claim 46 has been cancelled.

Claims 42 and 74 have been amended to remove reference to "a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test."

Claims 42 and 74 have been amended to specify that each microsphere conjugated to a specific capture antibody is spectrally distinct from a microsphere conjugated to a different capture antibody. This is supported in Figure 10, and described in paragraphs [0074] and [0089] of the specification.

**I. Claim Objections**

The Examiner has objected to Claim 46 as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 46 has been cancelled.

**II. Claim Rejections under 35 USC §112**

A. The Examiner has rejected Claims 42, 46, 51-53, 56, 57, and 74 under 35 USC §112, first paragraph, for failing to comply with the written description requirement due to the term, "a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test."

Claims 42 and 74 have been amended to remove reference to the term to which the Examiner has objected. Applicants believe that this will overcome the Examiner's rejection.

**B.** The Examiner has rejected Claims 42, 46, 51-53, 56, 57, and 74, stating that it is unclear how the first and second fluorophores are related to detection. Applicants have amended Claims 42 and 74 to specify that each microsphere conjugated to a specific capture antibody is spectrally distinct from a microsphere conjugated to a different capture antibody. This is supported in Figure 10, and described in paragraphs [0074] and [0089] of the specification.

In the currently disclosed assay, each microsphere is labeled internally with a fixed ratio of two different fluorophores (110 in Figure 10), which combine to generate a detectable fluorescent signal. This allows for creation of microspheres having a multitude of detection signals by creating microspheres with varying ratios of the two fluorophores. This is useful in multiplex assays because many microspheres with non-overlapping signals can be used, each to detect a different antigen.

Each microsphere is conjugated to a target LSD capture antibody (120 in Figure 10). When the target LSD antigen (130 in Figure 10) is present, the target LSD capture antibody (120 in Figure 10) binds it, and the detection LSD antibody (140 in Figure 10) also binds it. The detection LSD antibody (140 in Figure 10) is conjugated to a detection molecule (150 in Figure 10). In this situation (i.e. when the LSD antigen is present), two signals are detectable from the microsphere as it passes through a flow cytometer: 1) the signal from the fluorophores in the microsphere; and 2) the signal from the detection molecule. This allows indirect detection of the LSD antigen, because it is known to be present when the microsphere signal and the detection molecule are both present as the microspheres are processed in a flow cytometer. It is noted that while a flow cytometer presents one option for detecting such an assay, it would also be possible to detect the sandwich assay in other formats, including microtitre plates.

**III. Conclusion**

Applicants respectfully submit that, in light of the foregoing comments, all pending claims are in condition for allowance. A Notice of Allowance is therefore requested.

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,



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